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A NEW SYNTHESIS METHOD FOR PREGNENOLONE COMPOUNDS
[Yi zhong xin de yun xi tong chun hua he wu he cheng fang fa]

Weisheng Tian et al.

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INVENTORS	(72):	Weisheng Tian et al.
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1. A new synthesis method for pregnenolone compounds, characterized in that in a polar solvent, pseudosteroidal sapogenin, hydrogen peroxide, metal catalyst and organic or inorganic acid in molar ratio 1:1.0–4.0:0.001–1:0.0005–10 are reacted at 0–80°C for 0.1–24 h; the described steroidal sapogenins are diosgenin, tigogenin, timosaponin and hecogenin natural sapogenins or sapogenin-analog products formed through natural sapogenin modification; said metal catalyst is anhydrous wolframic acid, wolframate, anhydrous molybdic acid, molybdate, phosphomolybdate, heteropolyacid, and sodium heteropolyacid.

2. A new synthesis method for pregnenolone compounds according to Claim 1, characterized in that the described pseudosteroidal sapogenin, hydrogen peroxide, metal catalyst and acid are in a molar ratio 1:1 - 2:0.01–0.1:0.001–0.01.

3. A new synthesis method for pregnenolone compounds according to Claim 1, characterized in that the described organic acid is a carboxylic acid comprising acetic acid, formic acid, propionic acid, butyric acid, benzoic acid, substituted benzoic acid, phthalic acid, and M-phthalic acid and sulfonic acid and its derivatives comprising benzene sulfonic acid, methanesulfonic acid - benzene sulfonic acid, and fluorosulfonic acid.

4. A new synthesis method for pregnenolone compounds according to Claim 1, characterized in that the described inorganic acid is an inorganic acid comprising sulfuric acid, phosphoric acid and phosphorous acid.

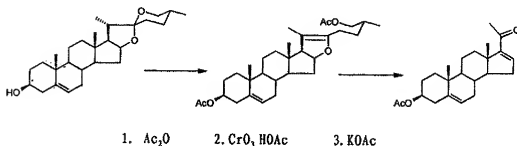
5. A new synthesis method for pregnenolone compounds according to Claim 1, characterized in that after reacting, the product is refluxed in potassium acetate/acetic acid for 1 h, and the pressure is reduced to remove a portion of the acetic acid and residue extracted using an organic solvent.

* [Numbers in right margin indicate pagination of the original text.]

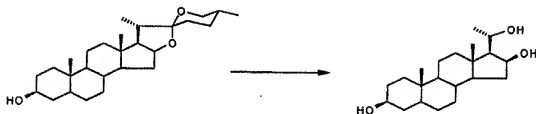
6. A new synthesis method for pregnenolone compounds according to Claim 1, characterized in that the described polar solvent is a proton or non-proton polar solvent comprising methylene halide, haloform, difluoromethane, acetic acid, tetrahydrofuran, ether, isopropyl ether, tert-butyl alcohol, dioxane, dimethyl sulfoxide, N, N-dimethyl formamide, acetone, butanone, acetonitrile, or ethyl acetate.

The present invention involves a new synthesis method for pregnenolone compounds, in an organic solvent hydrogen peroxide is used to catalyze and oxidize pseudosapogenin, to obtain pregnenolone and 3-methyl- δ -butyrolactone. /1

China has a wealth of steroidal sapogenin resources, for example, diosgenin, tigogenin, timogenin, and hecogenin; they are basic source materials for manufacturing various steroidal medications. In the use of steroidal sapogenin to synthesize steroidal medications, first the steroidal sapogenin must be broken down into pregnenolone compounds. To date, the main methods used in chemical laboratories and industrial manufacturing are still the chemical family marker provided breakdown methods (*J. Am. Chem. Soc.* 1947, 69, 2167). That is, in anhydrous acetic acid and acetic acid, pressure is applied at high temperature (200°C and above) to fragment the steroidal sapogenin to become the corresponding pseudosteroidal sapogenin, then oxidized using chromic anhydride and the reaction completed to supply the corresponding pregnenolone. Three-step total yield is about 60%. Using tigogenin as an example, the reaction formula is as follows:



After this, although this breakdown method was continually improved (Micovic I.V. *Synthesis*, 1990, 591), it still was not possible to change the disadvantages of said method. In fact, it was not possible to improve the breakdown process in the chromic anhydride removal oxidizing reaction, that is to say: in the steroidal sapogenin breakdown process, the environmental pollution issue still was unsolved. For this reason, starting in 1991 the inventors began to study a reasonable use of steroidal sapogenin resources. Previous research results: use of organic peroxide acid in steroidal sapogenin oxidation and basic hydrolytic synthesis of pregnenolone equivalent–pregnenolone method (Chinese Patent No. CN96116304.6). The two-step total yield may reach 90% or higher. Taking tigogenin as an example, the reaction formula is as follows:



The present inventors also studied the direct breakdown steroidal sapogenin provided to form the corresponding steroid–22- carboxylic acid–16–ester lactone method (Chinese Patent No. CN00127974.2);

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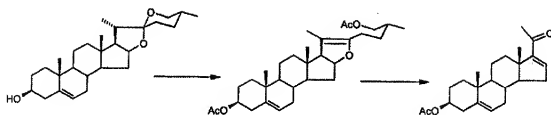


In the supplied methods for breaking down steroidal sapogenin, they implement use of hydrogen peroxide to replace chromic anhydride to break down steroidal sapogenin; however, the obtained breakdown product still could not be directly used in steroidal medication synthesis. In order to truly

solve the problem of environmental pollution during the steroidal sapogenin breakdown process, it is necessary to further study methods for using pregnenolone and steroidal-22-carboxylic acid-16-ester lactone to synthesize steroidal medications, or the use of hydrogen peroxide to replace chromic anhydride to break down steroidal sapogenin into the corresponding pregnenolone. In light of the fact that pregnenolone already serves as a key intermediate for steroidal medication synthesis and is already used in steroidal medication manufacturing, the public demands further advanced methods to satisfy market development needs.

The objective of the present invention is to supply a method to break down steroidal sapogenins into pregnenolone. Specifically speaking, it is a method that uses hydrogen peroxide to replace chromic anhydride to break down pseudosteroidal sapogenin into the corresponding pregnenolone and it achieves satisfactory results.

The method in the present invention uses an organic solvent, with a metal catalyst present or not present, using hydrogen peroxide to replace chromic anhydride in breaking down pseudosteroidal sapogenin, after the reaction the reductant is added to reduce excess oxidizing agent, then it undergoes the basic elimination reaction to supply the pregnenolone.



The specific operating steps of this method are as follows:

First, reference is made to existing manufacturing methods that use high-pressure fragmentation of steroidal sapogenin to form pseudosteroidal sapogenin. Then pseudosteroidal sapogenin oxidation is performed to remove the reaction and make it possible to obtain the pregnenolone product.

Pseudosteroidal sapogenin is dissolved in polar solvent, hydrogen peroxide, metal catalyst and acid added, pseudosteroidal sapogenin, hydrogen peroxide, metal catalyst and acid in molar ratio 1:1.0-4.0:0.001-1:0.0005-10; 1:1 - 2:0.01-0.1:0.001-0.01 is recommended. Reaction is performed at 0-80°C, reaction time is 0.1-24 h. Chromatographic reactions are tracked against the complete reactions of the original materials. After the reaction, it is possible to reflux in potassium acetate/acetic acid for 1 h to convert all the non-eliminated complete 16-ester-20-ketone into pregnenolone. The pressure is reduced to eliminate a portion of the acetic acid, the residue is extracted using cyclohexane, ether, petroleum ether and other organic solvents to extract, and processing of the extraction fluid obtains the needed pregnenolone. The mother liquid is processed to obtain 3-methyl- δ -butyrolactone.

The described steroidal sapogenins comprise: diosgenin, tigogenin, timogenin, hecogenin and other natural sapogenins and sapogenin analogs formed from modifications to natural sapogenins;

The described metal catalysts include: anhydrous wolframic acid, wolframate, anhydrous molybdic acid, molybdate, phosphomolybdate, heteropolyacid, and sodium heteropolyacid.

The described acids include: acetic acid, formic acid, methyl acetic acid, butyric acid, benzoic acid, replaced benzoic acid, phthalic acid, M-phthalic acid and other carboxylic acids; benzene sulfonic acid, methanesulfonic acid - benzene sulfonic acid, fluorosulfonic acid, and other sulfonic acids and their derivatives; sulfuric acid, phosphoric acid, phosphorous and other inorganic acids.

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The described polar solvents include: methylene halide, haloform, difluoromethane, acetic acid, tetrahydrofuran, ether, isopropyl ether, tert-butyl alcohol, dioxane, dimethylsulfoxide, N, N-dimethyl formamide, acetone, butanone, acetonitrile, ethyl acetate and other proton or non-proton polar solvents;

Reduction agents include: sodium sulfite, hydrosulfite of sodium, sodium pyrohydrosulfite, sodium hyposulfite, vat powder, et al.;

The following embodiments assist in explaining the present invention but do not limit the present invention.

Embodiment 1

Pseudohecogenin acetate and chromic anhydride oxidizing and breakdown reaction: 250 mg (0.5 mmol) pseudohecogenin acetate is dissolved in 1 mL of acetic acid, dropwise chromic anhydride acetic acid solution (112.5 mg (1.13 mmol) chromic anhydride is obtained by dissolving in 0.9 mL acetic acid) is added, it is stirred at room temperature to react for 2.5 h, 0.05 mL formaldehyde is added to dissolve excess oxidizing agents, 125 mg of potassium acetate are added, heated to 100°C, it is continuously stirred at room temperature to react for 1 h, and the reaction is terminated. The reaction mixture undergoes reduced pressure to evaporate out a portion of the acetic acid, after the residue is obtained ice is poured in, the precipitate precipitated out, it is filtered, washed, and dried to obtain the reaction crude product. The reaction crude product then undergoes silica gel chromatography layer precipitation (eluent: petroleum ether/ethyl acetate = 12/1) to obtain 118 mg broken-down pregnenolone acetate, yield 65.9%. m.p. 162-64°C, infrared spectrophotometry is performed (ν): 2924, 2846, 1737, 1675, 1587, 1243, 1031 cm^{-1} . Hydrogen nuclear magnetic resonance spectroscopy (300MHz, CDCl_3) δ : 6.60(dd, $J = 1.3\text{Hz}$, 1H, 16-H), 4.6(m, 1H, 3-H), 2.01(s, 3H, 3- $\text{CH}_3\text{COO}-$), 2.26(s, 3H, $\text{CH}_3\text{CO}-$, 21-H), 0.85(s, 3H, 18-H), 0.88(s, 3H, 19-H)ppm. Mass spectrum (m/z , %) 417(M+1), 373(10.60), 356(28.36), 281(15.65), 253(19.38), 43(100).

Embodiment 2

Pseudohecogenin acetate and catalyst-quantity chromic anhydride and hydrogen peroxide solution oxidizing and breakdown reaction: 250 mg (0.5 mmol) pseudohecogenin acetate is dissolved in 1 mL of

acetic acid, chromic anhydride (5 mg (0.05 mmol), hydrogen peroxide solution (30% H_2O_2 , 204 μL , 2 mmol) acetic acid (1 mL) solution. Reaction mixture is stirred at room temperature to react for 3 h, 125 mg potassium acetate and 2 mL saturated sodium bisulfite aqueous solution are added, continuously stirred at 100°C to react for 1 h, the pressure is reduced to evaporate out the acetic acid to obtain 180 mg reacted crude, then silica gel column precipitation is again performed to obtain 103 mg pregnenolone acetate, yield 57.5%. Spectral data is the same as that in Embodiment 1.

Embodiment 3

Pseudohecogenin acetate and hydrogen peroxide solution oxidizing and breakdown reaction: 250 mg (0.5 mmol) pseudohecogenin acetate is dissolved in 2 mL acetic acid and hydrogen peroxide solution (30% H_2O_2 , 204 μL , 2 mmol). The obtained reaction mixture is stirred to react at room temperature for 2.5 h, 125 mg potassium acetate and 2 mL saturated sodium bisulfite aqueous solution are added, continuously stirred at 100°C to react for 1 h, pressure is reduced to evaporate out most of the solvent, ice added, and CH_2Cl_2 extraction performed. The extraction fluid is washed, dried, and evaporated to obtain 303 mg crude product, it undergoes silica gel column precipitation (eluent: petroleum ether/ethyl acetate = 12/1) to obtain 80 mg broken-down pregnenolone acetate, yield 44.7%. Spectral data is the same as that in Embodiment 1.

Embodiment 4

Pseudohecogenin acetate and catalyst-quantity anhydrous molybdic acid and hydrogen peroxide solution oxidizing and breakdown reaction: 125 mg (0.25 mmol) pseudohecogenin acetate is dissolved in 2 mL of acetone, 7 mg (0.05 mmol) MoO_3 , 1 drop 4M H_3PO_4 , and hydrogen peroxide solution (30% H_2O_2 , 102 μL , 1 mmol) are added. The obtained reaction mixture is stirred to react at room temperature

for 6 h, if the original material is not reacted completely, it is reflux reacted again for 2 h, filtered to remove solids, as much filtrate as possible is evaporation dried, 2.5 mL water is added to dilute, CH_2Cl_2 extraction used, washed using saturated NaCl solution, after organic phase evaporation to remove the solvent, 0.5 mL HOAc and 63 mg KOAc are added, and refluxed 1 h. Pressure is reduced to evaporate out most of the solvent, ice is added, CH_2Cl_2 extraction is performed, the extraction fluid is washed, dried, and evaporated to obtain a crude product, which then undergoes silica gel column precipitation (eluent: petroleum ether/ethyl acetate = 10/1) to obtain 62 mg broken-down pregnenolone acetate, yield 68.8%. Spectral data is the same as that in Embodiment 1.

Embodiment 5

Pseudohecogenin acetate and catalyst-quantity anhydrous molybdic acid and hydrogen peroxide solution oxidizing and breakdown reaction: 500 mg (1 mmol) pseudohecogenin acetate is dissolved in 8 mL of acetone, 46 mg (0.2 mmol) WO_3 , 4 drops 4M H_3PO_4 , and hydrogen peroxide solution (30% H_2O_2 , 408 μL , 4 mmol) are added. The obtained reaction mixture is stirred to reflux react for 6 h, filtered to remove solids, as much filtrate as possible is evaporated, 10 mL of water added to dilute, CH_2Cl_2 extraction used, washed using saturated NaCl solution, after organic phase evaporation removal of the solvent, 2 mL HOAc and 250 mg KOAc are added and refluxed 1 h. The pressure is reduced to evaporate out most of the solvent, ice is added, CH_2Cl_2 extraction is used, the extraction fluid is washed, dried, and evaporated to obtain the crude product, silica gel column precipitation is performed (eluent: petroleum ether/ethyl acetate = 10/1) to obtain 205 mg broken-down pregnenolone acetate, yield 58.7%. Spectral data is the same as that in Embodiment 1.

Embodiment 6

Pseudohecoenin acetate and catalyst-quantity molybdate and hydrogen peroxide solution oxidizing and breakdown reaction: 500 mg (1 mmol) pseudohecoenin acetate is dissolved in 8 mL of acetone, 48 mg (0.2 mmol) $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$, 4 drops 4M H_3PO_4 , and hydrogen peroxide solution (30% H_2O_2 , 408 μL , 4 mmol) are added. The obtained reaction mixture is stirred to reflux react at room temperature for 2.5 h, filtered to remove solids, as much filtrate as possible is evaporation dried, 10 mL of water added to dilute, CH_2Cl_2 extraction performed, washed using saturated NaCl solution, after organic phase evaporation removal of the solvent, 2 mL HOAc and 250 mg KOAc are added, and refluxed 1 h. The pressure is reduced to evaporate out most of the solvent, ice is added, CH_2Cl_2 extraction is performed, extraction fluid is washed, dried, and evaporated out to obtain a crude product, silica gel column precipitation is performed (eluent: petroleum ether/ethyl acetate = 10/1) to obtain 228 mg broken-down product pregnenolone acetate, yield 63.4%. Spectral data is the same as that in Embodiment 1.

Embodiment 7

Pseudohecoenin acetate and catalyst-quantity wolframate and hydrogen peroxide solution oxidizing and breakdown reaction: 500 mg (1 mmol) pseudohecoenin acetate is dissolved in 8 mL of acetone, 66 mg (0.2 mmol) $\text{Na}_2\text{WO}_4 \cdot 2\text{H}_2\text{O}$, 4 drops 4M H_3PO_4 , and hydrogen peroxide solution (30% H_2O_2 , 408 μL , 4 mmol) are added. The obtained reaction mixture is stirred to reflux react at room temperature for 0.5 h, filtered to remove solids, as much filtrate as possible is evaporated dry, 10 mL water added to dilute, CH_2Cl_2 extraction performed, washed using saturated NaCl solution, after organic phase evaporation removal of solvent, 2 mL HOAc and 250 mg KOAc are added and refluxed 1 h. Pressure is reduced to evaporate out most of the solvent, ice is added, CH_2Cl_2 extraction is performed, extraction fluid is washed, dried, and evaporated to obtain a crude product, silica gel column precipitation

performed (eluent: petroleum ether/ethyl acetate = 10/1) to obtain 180 mg broken-down pregnenolone acetate, yield 59.2%. Spectral data is the same as that in Embodiment 1.

Embodiment 8

Pseudohecogenin acetate and catalyst-quantity wolframate and hydrogen peroxide solution oxidizing and breakdown reaction: 125 mg (0.25 mmol) pseudohecogenin acetate are dissolved in 1 mL of dioxane, 8 mg (0.024 mmol) $\text{Na}_2\text{WO}_4 \cdot 2\text{H}_2\text{O}$, 1 drop 4M H_3PO_4 , and hydrogen peroxide solution (30% H_2O_2 , 102 μL , 1 mmol) added. The obtained reaction mixture is stirred to react at room temperature for 3 days. It is filtered to remove solids, as much filtrate as possible is evaporated dry, 2.5 mL water is added to dilute, CH_2Cl_2 extraction is performed, is washed using saturated NaCl solution, after organic phase evaporation removal of solvent, 0.5 mL HOAc and 63 mg KOAc are added and refluxed for 1 h. The pressure is reduced to evaporate out most of the solvent, ice is added, CH_2Cl_2 extraction is performed, extraction fluid is washed, dried, and evaporated to obtain a crude product, silica gel column precipitation performed (eluent: petroleum ether/ethyl acetate = 10/1) to obtain 63 mg broken-down pregnenolone acetate, yield 70%. Spectral data is the same as that in Embodiment 1. /5

Embodiment 9

Pseudohecogenin acetate and catalyst-quantity wolframate and hydrogen peroxide solution oxidizing and breakdown reaction: 500 mg (1 mmol) pseudohecogenin acetate, 4 mL tert-butyl alcohol, 33 mg (0.1 mmol) $\text{Na}_2\text{WO}_4 \cdot 2\text{H}_2\text{O}$, 4 drops 4M H_3PO_4 , and hydrogen peroxide solution (30% H_2O_2 , 408 μL , 4 mmol) are added to a reaction vessel. The obtained reaction mixture is stirred in a 50°C oil bath to react for 5.5 h. Solids are filtered out, as much filtrate as possible is evaporated dry, 10 mL of water is added to dilute, CH_2Cl_2 extraction is performed, then washed using saturated NaCl solution, and after

organic phase evaporation removal of the solvent, 2 mL HOAc and 250 mg KOAc are added and refluxed for 1 h. The pressure is reduced to evaporate out most of the solvent, ice is added, CH₂Cl₂ extraction is performed, the extraction fluid is washed, dried, and evaporated to obtain crude product, silica gel column precipitation performed (eluent: petroleum ether/ethyl acetate = 10/1) to obtain 298 mg broken-down pregnenolone acetate, yield 82%. Spectral data is the same as that in Embodiment 1.

Embodiment 10

Pseudohecogenin acetate and catalyst-quantity anhydrous molybdic acid and hydrogen peroxide solution oxidizing and breakdown reaction: 250 mg (0.5 mmol) pseudohecogenin acetate, 2 mL tert-butyl alcohol, 29 mg (0.2 mmol) MoO₃, 122 mg (1 mmol) C₆H₅CO₂H, and hydrogen peroxide solution (30% H₂O₂, 204 µL, 2 mmol) are added to a reaction vessel. The obtained reaction mixture is stirred in a 50°C oil bath to react for 4 h. It is filtered to remove solids, as much filtrate as possible is evaporated dry, 10 mL of water is added to dilute, CH₂Cl₂ extraction performed, washed using saturated NaCl solution, after organic phase evaporation removal of solvent, 1 mL HOAc and 125 mg KOAc are added and refluxed for 1 h. Pressure is reduced to evaporate out most of the solvent, ice is added, CH₂Cl₂ extraction is performed, the extraction fluid is washed, dried, and evaporated to obtain crude product, silica gel column precipitation is performed (eluent: petroleum ether/ethyl acetate = 10/1) to obtain 156 mg broken-down pregnenolone acetate, yield 87.6%. Spectral data is the same as that in Embodiment 1.

Embodiment 11

Pseudohecogenin acetate and catalyst-quantity anhydrous molybdic acid and hydrogen peroxide solution oxidizing and breakdown reaction: 500 mg (1 mmol) pseudohecogenin acetate, 4 mL tert-butyl

alcohol, 58 mg (0.4 mmol) MoO_3 , 166 mg (1 mmol) M-phthalic acid, and hydrogen peroxide solution (30% H_2O_2 , 408 μL , 4 mmol) are added to a reaction vessel. The obtained reaction mixture is stirred in a 35°C oil bath to react for 3.5 h. Saturated NaHSO_3 solution is added to remove excess H_2O_2 , it is filtered, the filtrate evaporation dried, excess material extracted using cyclohexane, the extraction fluid evaporation dried, 4 mL HOAc and 250 mg KOAc added and reflux reacted for 2 h. The pressure is reduced to evaporate out most of the solvent, ice is added, CH_2Cl_2 extraction is performed, the extraction fluid is washed, dried, and evaporated to obtain 506 mg crude product, silica gel column precipitation performed (eluent: petroleum ether/ethyl acetate = 10/1) to obtain 239 mg broken-down pregnenolone acetate, yield 67.1%. Spectral data is the same as that in Embodiment 1.

Embodiment 12

Pseudohecogenin acetate and catalyst-quantity phosphoric molybdic acid and hydrogen peroxide solution oxidizing and breakdown reaction: 500 mg (1 mmol) pseudohecogenin acetate is dissolved in 2 mL acetone, 186 mg $\text{H}_7[(\text{PMO}_2\text{O}_7)_6] \times \text{H}_2\text{O}$ (0.1mmol), 4 drops of 4M H_3PO_4 , and hydrogen peroxide solution (30% H_2O_2 , 408 μL , 4 mmol) are added. The obtained reaction mixture is stirred at room temperature to react for 4 h, if the original material has not completed reaction, it is stirred continuously in a 60°C oil bath to react for 3 h, filtered to remove the solids, as much filtrate as possible evaporated, 10 mL water is added to dilute, the CH_2Cl_2 extraction performed, washed using saturated NaCl solution, after the organic-phase evaporation removal of solvent, 4 mL HOAc and 250 mg KOAc are added and refluxed for 1 h. Pressure is reduced to evaporate out most of the solvent, ice is added, CH_2Cl_2 extraction performed, the extraction fluid is washed, dried, and evaporated to obtain crude product, silica gel column precipitation is performed (eluent: petroleum ether/ethyl acetate = 10/1) to obtain 301 mg

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broken-down product pregnenolone acetate, yield 84%. Spectral data is the same as that in Embodiment 1.

Embodiment 13

Pseudotimogenin acetate and catalyst-quantity anhydrous molybdic acid and hydrogen peroxide solution oxidizing and breakdown reaction: 250 mg (0.5 mmol) pseudotimogenin acetate, 2 mL tert-butyl alcohol, 29 mg MoO_3 (0.2 mmol), 122 mg $\text{C}_6\text{H}_5\text{CO}_2\text{H}$ (1 mmol), and hydrogen peroxide solution (30% H_2O_2 , 204 μL , 2 mmol) are added to a reaction vessel. The obtained reaction mixture is stirred in a 50°C oil bath to react for 4 h. It is filtered to remove solids, as much filtrate as possible is evaporation dried, 10 mL water is added to dilute, CH_2Cl_2 extraction is performed, it is washed using saturated NaCl solution, after organic phase evaporation removal of solvent 1 mL HOAc and 125 mg KOAc are added and refluxed for 1 h. The pressure is reduced to evaporate out most of the solvent, ice is added, CH_2Cl_2 extraction is performed, the extraction fluid is washed, dried, and evaporated to obtain crude product, silica gel column precipitation is performed (eluent: petroleum ether/ethyl acetate = 10/1) to obtain 150 mg broken-down 5 β -pregnenolone acetate, yield 83.8%. m.p. 144-6°C, infrared spectrophotometry is performed (ν): 2924, 2845, 1738, 1674, 1586, 1245, 1030 cm^{-1} . Hydrogen nuclear magnetic resonance spectroscopy (300MHz, CDCl_3) δ : 6.61(dd, J = 1.3Hz, 1H, 16-H), 4.62(m, 1H, 3-H), 2.01(s, 3H, 3- $\text{CH}_3\text{COO}-$), 2.26(s, 3H, $\text{CH}_3\text{CO}-$, 21-H), 0.84(s, 3H, 18-H), 0.88(s, 3H, 19-H)ppm. Mass spectra (m/z, %) 417 (M+1), 373(10.60), 356(28.36), 281(15.65), 253(19.38), 43(100).

Embodiment 14

Pseudodiosgenin acetate and catalyst-quantity wolframate and hydrogen peroxide solution oxidizing and breakdown reaction: 500 mg (1 mmol) pseudodiosgenin acetate, 4 mL tert-butyl alcohol, 33 mg

$\text{Na}_2\text{WO}_4 \cdot 2\text{H}_2\text{O}$ (0.1 mmol), 4 drops 4M H_3PO_4 , and hydrogen peroxide solution (30% H_2O_2 , 408 μL , 4 mmol) are added to a reaction vessel. The obtained reaction mixture is stirred in a 50°C oil bath to react for 5.5 h. It is filtered to remove solids, as much filtrate as possible is evaporation dried, 10 mL water is added to dilute, CH_2Cl_2 extraction is performed, washed using saturated NaCl solution, after organic phase evaporation removal of solvent, 2 mL HOAc and 250 mg KOAc are added and refluxed for 1 h. The pressure is reduced to evaporate out most of the solvent, ice is added, CH_2Cl_2 extraction is performed, the extraction fluid is washed, dried, and evaporated to obtain crude product, silica gel column precipitation is performed (eluent: petroleum ether/ethyl acetate = 10/1) to obtain 297 mg broken-down pregnadienolone acetate, yield 82%. m.p. 176°C, infrared spectrophotography is performed (ν): 2966, 2945, 1731, 1662, 1585, 1248, 1234, 1030 cm^{-1} . Hydrogen nuclear magnetic resonance spectroscopy (300MHz, CDCl_3) δ : 6.61(dd, J = 1.3Hz, 1H, 16-H), 5.04(d, J = 4Hz, 1H, 6-H), 4.62(m, 1H, 3-H), 2.01 (s, 3H, 3- $\text{CH}_3\text{COO}-$), 2.26(s, 3H, $\text{CH}_3\text{CO}-$, 21-H), 0.84(s, 3H, 18-H), 0.88(s, 3H, 19-H)ppm. Mass spectra (m/z, %) 415 (M+1), 371(10.60), 354(28.36), 279(15.65), 251(19.38), 43(100).

Embodiment 15

Pseudorockogenin acetate and catalyst-quantity anhydrous molybdic acid and hydrogen peroxide solution oxidizing and breakdown reaction: 129 mg (0.25 mmol) pseudorockogenin acetate is dissolved in 2 mL acetone, 7 mg MoO_3 (0.05 mmol), 1 drop 4M H_3PO_4 , and hydrogen peroxide solution (30% H_2O_2 , 102 μL , 1 mmol) are added. The obtained reaction mixture is stirred at room temperature to react for 6 h, if the original material is not completely reacted, then it is reflux reacted again for 2 h, filtered to remove solids, as much filtrate as possible is evaporation dried, 2.5 mL water is added to dilute, CH_2Cl_2 extraction is performed, it is washed using saturated NaCl solution, after organic phase evaporation removal of solvent 0.5 mL HOAc and 63 mg KOAc are added and refluxed for 1 h. The pressure is

reduced to evaporate out most of the solvent, ice is added, CH_2Cl_2 extraction is performed, the extraction fluid is washed and dried, evaporation dried to obtain crude product, silica gel column precipitation performed (eluent: petroleum ether/ethyl acetate = 10/1) to obtain 62 mg broken-down 12 β -acetoxy pregnenolone acetate, yield 68.8%. m.p. 214-5°C, infrared spectrophotometry is performed (ν): 2925, 2847, 1737, 1675, 1587, 1363, 1243, 1031, 984, 824, 635cm^{-1} . Hydrogen nuclear magnetic resonance spectroscopy (300MHz, CDCl_3) δ : 6.60(dd, $J = 1.3\text{Hz}$, 1H, 16-H), 4.68(dd, $J = 11.3$, 4.6Hz, 1H, 12-H), 4.6(m, 1H, 3-H), 2.01 (s, 3H, 3- $\text{CH}_3\text{COO}-$), 2.04(s, 3H, $\text{CH}_3\text{COO}-$), 2.26(s, 3H, $\text{CH}_3\text{CO}-$, 21-H), 0.88(s, 3H, 19-H)ppm. Mass spectra (m/z , %) 417 ($M+1$), 373(10.60), 356(28.36), 281(15.65), 253(19.38), 43(100).

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